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Glycol Ethers and Neurodevelopment: Investigating the Impact of Prenatal Exposures

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Glycol ethers have been widely used since the 1960s as solvents and stabilizers in a variety of personal, household, and industrial products.[1] A new study in *Environmental Health Perspectives* provides some of the first evidence of associations between prenatal exposures to glycol ethers and cognitive impairments in children.[2]These chemicals are generally valued for their low acute toxicity. However, the European Union has restricted[3] the use of several glycol ethers due to concerns about potential reproductive toxicity and other health risks.[1]

In the current study, researchers in France measured five glycol ether metabolites in urine samples from 204 pregnant women, which had been collected between 2002 and 2006 for the broader PELAGIE mother–child cohort.[4] At age 6, their children were given a series of neurocognitive tests to assess verbal comprehension, working memory, and visuospatial ability.

All the women had detectable levels in their urine of the metabolites phenoxyacetic acid (PhAA) and 2-butoxyacetic acid (BAA, a by-product of two restricted glycol ethers used in hair dyes and spray paints and cleaners). Nearly all women also had detectable levels of ethoxyacetic acid (EAA), ethoxyethoxyacetic acid (EEAA), and methoxyacetic acid (MAA). The authors note that this high frequency of detection and the relatively short half-life of these metabolites in the body (6–80 hours) suggest that exposures are not only common but also repeated.[2]

After adjusting for potential confounders, including the mother's intelligence and the amount of cognitive and emotional stimulation the child received at home, the researchers found that higher verbal comprehension scores among the children were associated with lower levels of PhAA in their mothers' urine during pregnancy. PhAA is the primary metabolite of 2-phenoxyethanol (EGPhE), a glycol ether commonly used in perfumes, cosmetics, lotions, and other personal care products.[2]

Glycol ethers are excreted relatively quickly, so when studying the health effects of these compounds, it matters when samples are collected. First-morning urine samples, for instance, would not capture glycol ether exposures from products used during the day. © ShotShare/iStockphoto.

The researchers also reported a weaker association between a mother's urinary levels of EAA in pregnancy and her child's ability to copy simple drawings.[2] This compound is a metabolite of glycol ethers commonly used in cleaning products.

Lead author Rémi Béranger, a midwife and postdoctoral researcher with the French National Institute of Health and Medical Research, is not aware of any previous studies in this area. "We strongly need other studies to investigate the same question, because the evidence is insufficient right now," he says. "I know that researchers always say that, but because of the limited evidence of biological plausibility we really need additional studies."

The authors note several limitations. For one, they had only a single urine sample per woman, offering limited information because glycol ether metabolites clear from the body relatively rapidly. Urine samples collected upon waking, for instance, would not capture exposures resulting from applying cosmetics later in the morning.[2]

In addition, the results possibly could be explained by exposure to preservatives or other chemicals often used in conjunction with glycol ethers,[2] including parabens, sodium benzoate, and methyldibromoglutaronitrile.[5] Little is known about whether exposures to these chemicals may be associated with neurodevelopmental outcomes in the children of mothers with such exposures.

Studies of prenatal exposure to organic solvents in general (as opposed to glycol ethers in specific, which are one group in the larger family) have found higher maternal occupational exposure during pregnancy to be associated with reduced visual ability[6,7] and neurobehavioral performance[8,9] in children. Another study reported a relationship between organic solvent exposure and visual–motor ability, the same skill shown in the present study to be slightly depressed in children whose mothers had the highest urinary levels of EAA.[10]

York University professor Christine Till, lead author of the latter paper, says that the new work by Béranger et al. is "a direct replication of what we were finding." She adds, "I was impressed overall by the methodology, and it is interesting to see the findings replicate what we reported."

Future research into possible neurodevelopmental toxicity of glycol ethers should target potential mechanisms, such as oxidative stress and impacts on neurotransmitters, as well as [provide] better understanding of how populations are exposed to the chemicals, says senior author and PELAGIE principal investigator Cecile Chevrier.

The study also highlights the need for more research into cognitive outcomes associated with early life chemical exposures in general, according to Paule Vasseur, professor at France's University of Lorraine, who was not involved in the study. "The consequences of chemical exposure during pregnancy are very poorly known, and the chemicals responsible for neurocognitive effects sparsely identified," she says. "This is a goal for the coming years."

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